DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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July 17, 2015

SIEMENS HEALTHCARE DIAGNOSTICS, INC.
FATIMA PACHECO
REGULATORY CLINICAL AFFAIRS SPECIALIST
511 BENEDICT AVENUE
TARRYTOWN NY 10591

Re: K143687
Trade/Device Name: ADVIA Centaur® Follicle Stimulating Hormone (FSH) Master Curve Material,
ADVIA Centaur® FT4 Master Curve Material,
ADVIA Centaur® T4 Master Curve Material,
ADVIA Centaur® T3 Master Curve Material
Regulation Number: 21 CFR 862.1660
Regulation Name: Quality control material (assayed and unassayed)
Regulatory Class: I, Reserved
Product Code: JJX
Dated: June 01, 2015
Received: June 02, 2015

Dear Fatima Pacheco:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements

as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Courtney H. Lias -S

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
k143687

Device Name
ADVIA Centaur® Follicle Stimulating Hormone (FSH) Master Curve Material

Indications for Use *(Describe)*
The ADVIA Centaur® Follicle Stimulating Hormone (FSH) Master Curve Material is for in vitro diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur FSH assay.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
k143687

Device Name
ADVIA Centaur® FT4 Master Curve Material

Indications for Use *(Describe)*
The ADVIA Centaur® Free thyroxine (FT4) Master Curve Material is for in vitro diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur FT4 assay.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

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Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
k143687

Device Name
ADVIA Centaur® T4 Master Curve Material

Indications for Use *(Describe)*
The ADVIA Centaur® Thyroxine (T4) Master Curve Material is for in vitro diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur T4 assay.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
k143687

Device Name
ADVIA Centaur® T3 Master Curve Material

Indications for Use *(Describe)*
The ADVIA Centaur® Triiodothyronine (T3) Master Curve Material is for in vitro diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur T3 assay.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

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Section 006: 510(k) Summary

510(k) Summary – ADVIA Centaur FSH Master Curve Material

Introduction: According to the requirements of 21 CFR 807.92, the following information provides sufficient details to understand the basis for determination of substantial equivalence.

The assigned 510(k) Number: k143687

1. Applicant Information	Siemens Healthcare Diagnostics Inc.
Mailing Address:	511 Benedict Avenue Tarrytown, NY 10591 USA
Contact Person:	Fatima Pacheco Regulatory Clinical Affairs Specialist
Phone Number:	(914) 524-2450
Fax Number:	(914) 524-3579
E-mail Address:	fatima.pacheco@siemens.com
Date Prepared:	July 13, 2015
2. Device Name	
Proprietary Name:	**ADVIA Centaur® Follicle Stimulating Hormone (FSH)**
Measurand:	**Master Curve Material**
Type of Test:	Quality Control materials for ADVIA Centaur FSH assay Master Curve Material (MCM) for ADVIA Centaur FSH assay
Regulation Section:	21 CFR 862.1660, Quality Control Material
Classification:	Class I Reserved
Products Code:	JJX–Single (Specified) Analyte Controls (Assayed and Unassayed)
Panel:	Clinical Chemistry (75)
3. Predicate Device Name	IMMULITE 2000 FSH Calibration Verification Material (CVM)
Predicate 510(k) No:	k133124
4. Device Description:	ADVIA Centaur® FSH Master Curve Material is an *in vitro* diagnostic product containing various levels of follicle-stimulating hormone spiked in lyophilized equine serum with sodium azide (0.1% after reconstitution) and preservatives. Each set contains eight levels (MCM1–8); with a reconstituted

	volume of 1.0 mL/vial per level. MCM1contains no analyte. The MCMs assigned values are lot-specific of target values: 0.00, 1.50, 4.50, 12.0, 30.0, 62.5, 130, 225 mIU/mL.
5. Intended Use: **Indication for Use:**	See Indications for Use Statement below: The ADVIA Centaur® Follicle Stimulating Hormone (FSH) Master Curve Material is for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur FSH assay.
Special Conditions for Use Statement(s):	For prescription use only
Special Instrument Requirements:	ADVIA Centaur® Systems A description of the ADVIA Centaur system is documented in k971418. Subsequent modifications to the instrument have been reviewed and cleared in k032525 and k041133.
6. Technological Characteristics and Substantial Equivalence Comparison with Predicate:	A comparison of the device features, intended use, and other information demonstrates that the ADVIA Centaur FSH MCM is substantially equivalent to the predicate device as summarized in **Table 1**.

Table 1: *Substantial Equivalence Comparison*

SIMILARITIES		
	Candidate Device	**Predicate Device**
Item	ADVIA Centaur FSH MCM	IMMULITE 2000 FSH Calibration Verification Material (CVM)
Intended Use	The ADVIA Centaur Follicle Stimulating Hormone (FSH) Master Curve Material is for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur FSH assay.	The IMMULITE FSH Calibration Verification Material (CVM) is for *in vitro* diagnostic use in the verification of calibration of the IMMULITE FSH assay on the IMMULITE 2000systems.
Analyte	Follicle stimulating Hormone	Same
Matrix	Equine serum	Bovine serum
DIFFERENCES		
Use	Multiple Use	Single Use
Form	Lyophilized	Liquid
Storage	2–8°C	≤ -20°C
Levels	8	4
Stability	**Unopened** – Stable when stored unopened at 2–8°C for 6 months. **Opened (Reconstituted)** – Stable when stored at 2–8°C for 28 days; or on-board for 4 hours.	**Unopened** – Stable at ≤ -20°C up to the expiration date.

7. Standard/Guidance Document References

The following recognized standard and guidance documents were used:

- Guidance for Industry – Abbreviated 510(k) Submissions for In Vitro Diagnostic Calibrators
- Guidance for Industry and FDA Staff – Assayed and Unassayed Quality Control Material

8. Test Principle

The MCMs are specifically intended for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur assays for use on the ADVIA Centaur systems. Customers may use MCMs for bi-annual calibration verification checks of the assay range and linearity in order to meet the requirements of hospital accreditation bodies.

9. Performance Characteristics

9.1 Analytical performance:

The following studies are not applicable for the purpose of this submission:

- *Precision/Reproducibility*
- *Linearity/Assay Reportable Range*
- *Detection limit*
- *Analytical Specificity*
- *Assay cut-off*
- *Method Comparison Studies*
- *Clinical Studies (Sensitivity, Specificity, and cut-off)*

9.2 Non-Clinical Performance Testing

9.2.1 *Stability Studies*

Stability studies were conducted on the ADVIA Centaur XP system to support the shelf life (unopened) and reconstituted material for the ADVIA Centaur FSH MCMs to ensure that it maintains optimal product performance throughout the established shelf-life. The data supports the stability claims detailed in the ADVIA Centaur FSH MCM Instructions for Use.

The following stability studies were performed for ADVIA Centaur FSH MCM:

- Real Time/Shelf Life (unopened) Stability
- In Use Open Vial (reconstituted) stored at 2–8°C Stability
- On-Board Stability

Real time shelf-life studies (unopened): Test FSH MCMs were stored unopened at 2–8°C and tested at T=0 and at the following time points: 7 months and 10 months. Real time studies are on-going at T=14 months, 18 months, 21 months, 24 months, and 25 months. Shelf life claims are based upon real time stability carried out one month after the duration claimed. Real time shelf-life stability studies of MCMs were determined by comparison of dose recoveries to -80°C reference MCMs. Current testing meets the sponsor's acceptance criteria for the real-time stability study up to the 7 months' time point, which supports a shelf-life claim of 6 months. Storage shelf-life (unopened) at 2–8°C is indicated by the expiration date on the vial label.

In-Use Open Vial (Reconstituted): Test FSH MCMs were reconstituted, each level pooled, aliquotted and stored at 2–8°C, tested in 5 replicates per level at T=0, 7, 14, 21, 28, and 29 days. The sponsor's acceptance criteria for the open vial (reconstituted) stability study were met to the 29 days' time point, which supports the open vial claim of 28 days when properly stored at 2–8°C.

On-board Stability: Pooled aliquots of test FSH MCMs in sample cups were stored on the ADVIA Centaur system and measured at time point T=0, 2, 4 and 5 hours. On-board stability studies of MCMs were determined by comparison of dose recoveries to the T=0 dose recovery results. The on-board stability study met the sponsor's acceptance criteria at the 5 hours' time point, which supports the on-board stability claim for 4 hours.

Stability Acceptance Criteria

The sponsor's stability specifications acceptance criteria for the ADVIA Centaur FSH MCM are as follows:

- Real Time/Shelf life (Unopened): The dose recovery for MCM1 and the % dose recoveries for MCM2–8 met the sponsor's required acceptance criteria.
- In-Use Open Vial (Reconstituted): The dose recovery for MCM1 and the % dose recoveries for MCM2–8 met the sponsor's required acceptance criteria.
- On-Board: The dose recovery for MCM1 and the % dose recoveries for MCM2–8 met the sponsor's required acceptance criteria.

9.2.2 *Value Assignment*

The ADVIA Centaur FSH MCMs are value assigned using assigned reference calibrators and MCMs. The assigned reference calibrators are prepared using follicle-stimulating hormone stock and are traceable to internal material which is standardized against World Health Organization (WHO) 2nd International Standard for human FSH (IS 94/632) reference material. The MCMs are manufactured using qualified materials and measurement procedures.

The new MCM doses must fall within the final value assignment specification for FSH MCMs. The MCMs dose values are generated using the two-point calibration. The new MCM dose is calculated based on the relationship between the observed reference MCM dose and its assigned value. A performance verification run consisting of 6 replicates of each MCM level is run using one instrument, one reagent kit lot and Bio-Rad controls. The mean MCM doses of the new MCM lot manufactured must fall within the customer range specifications.

The target for MCM1 is assigned a 0.0 dose. MCM1 is analyte-free basepool comprising of only the matrix and preservatives. The quality control specifications and final value assignment limits for FSH MCM ensure that MCM1 measures at or below the FSH assay sensitivity limit. MCM8 targeted greater than the assay range is diluted with the MCM1 to meet the reportable range of the assay.

9.2.3 *Expected Values*

The expected values are the lot-specific assigned values obtained at value assignment and the lot-specific assigned ranges are the lot-specific customer ranges established per the sponsor's internal procedural specifications for FSH MCM.

ADVIA Centaur FSH MCM levels and target values are provided in **Table 2.**

Table 2: *Example FSH MCM Levels and Target Values*

MCM level	Target Values (mIU/mL)
MCM1	0.00
MCM2	1.50
MCM3	4.50
MCM4	12.0
MCM5	30.0
MCM6	62.5
MCM7	130
MCM8	225
Assay Range	0.3–200 mIU/mL

9.2.4 *Traceability*

The ADVIA Centaur FSH assay is standardized against World Health Organization (WHO) 2nd International Standard for human FSH (IS 94/632) reference material based on the following correlation:
ADVIA Centaur FSH = 0.91 (WHO) – 0.18 mIU/mL
r = 0.999
Assigned values for calibrators and MCMs are traceable to this standardization.

10. Proposed Labeling

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

11. Conclusion

The ADVIA Centaur FSH Master Curve Material (MCM) is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the currently marketed IMMULITE 2000 FSH Calibration Verification Material (CVM). Based on the testing completed and the comparisons with predicate device, the ADVIA Centaur FSH Master Curve Material does not raise any new questions on safety and effectiveness and the results support a determination of substantial equivalence.

510(k) Summary – ADVIA Centaur FT4 Master Curve Material

Introduction: According to the requirements of 21 CFR 807.92, the following information provides sufficient details to understand the basis for determination of substantial equivalence.

The assigned 510(k) Number: k143687

1. Applicant Information	
Mailing Address:	Siemens Healthcare Diagnostics Inc. 511 Benedict Avenue Tarrytown, NY 10591 USA
Contact Person:	Fatima Pacheco Regulatory Clinical Affairs Specialist
Phone Number:	(914) 524-2450
Fax Number:	(914) 524-3579
E-mail Address:	fatima.pacheco@siemens.com
Date Prepared:	July 13, 2015
2. Device Name	
Proprietary Name:	**ADVIA Centaur® FT4 Master Curve Material**
Measurand:	Quality Control materials for ADVIA Centaur FT4 assay
Type of Test:	Master Curve Material (MCM) for ADVIA Centaur FT4 assay
Regulation Section:	21 CFR 862.1660, Quality Control Material
Classification:	Class I Reserved
Products Code:	JJX – Single (Specified) Analyte Controls (Assayed and Unassayed)
Panel:	Clinical Chemistry (75)
3. Predicate Device Name **Predicate 510(k) No:**	IMMULITE 2000 FT4 Calibration Verification Material (CVM) k140818
4. Device Description:	ADVIA Centaur® FT4 Master Curve Material is an *in vitro* diagnostic product containing various levels of thyroxine in human plasma with sodium azide. Each set contains seven levels; with a reconstituted volume of 1.0 mL/vial per level. MCM1 contains no analyte. The FT4 MCMs assigned values are lot-specific of target values: 0.00, 2.00, 5.00, 10.0, 15.0, 22.0, and 35.0 µg/dL which corresponds to FT4 values of 0.00, 0.42, 0.80, 1.70, 3.0, 5.6, and 13.5 ng/dL.
5. Intended Use: **Indication for Use:**	See Indications for Use Statement below: The ADVIA Centaur® Free thyroxine (FT4) Master Curve Material is for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur FT4 assay.

Special Conditions for Use Statement(s):	For prescription use only
Special Instrument Requirements:	ADVIA Centaur® Systems A description of the ADVIA Centaur system is documented in k971418. Subsequent modifications to the instrument have been reviewed and cleared in k032525 and k041133.
6. Technological Characteristics and Substantial Equivalence Comparison with Predicate:	A comparison of the device features, intended use, and other information demonstrates that the ADVIA Centaur FT4 MCM is substantially equivalent to the predicate device as summarized in **Table 1**.

Table 1: *Substantial Equivalence Comparison*

SIMILARITIES		
	Candidate Device	**Predicate Device**
Item	ADVIA Centaur FT4 MCM	IMMULITE 2000 FT4 Calibration Verification Material (CVM)
Intended Use	The ADVIA Centaur Free thyroxine (FT4) MCM is for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur FT4 assay.	The IMMULITE Free T4 Calibration Verification Material (CVM) is for *in vitro* diagnostic use in the verification of calibration of the IMMULITE Free T4 assay on the IMMULITE 2000 systems.
Analyte	Free thyroxine	Same
Form	Lyophilized	Same
Matrix	Human plasma	Human serum
DIFFERENCES		
Use	Multiple Use	Single Use
Storage	2–8°C	≤ -20°C
Levels	7	4
Stability	**Unopened** – Stable when stored unopened at 2–8°C for 6 months. **Opened (Reconstituted)** – Stable when stored at 2–8°C for 14 days; or on-board for 4 hours.	**Unopened** – Stored at ≤ -20°C until the expiration date. **Opened (Reconstituted)** – Stable for 8 hours at 15–25°C.

7. Standard/Guidance Document References

The following recognized standard and guidance documents were used:

- Guidance for Industry – Abbreviated 510(k) Submissions for In Vitro Diagnostic Calibrators
- Guidance for Industry and FDA Staff – Assayed and Unassayed Quality Control Material

8. Test Principle

The MCMs are specifically intended for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur assays for use on the ADVIA Centaur systems. Customers may use MCMs for bi-annual calibration verification checks of the assay range and linearity in order to meet the requirements of hospital accreditation bodies.

9. Performance Characteristics

9.1 Analytical performance:

The following studies are not applicable for the purpose of this submission:

- *Precision/Reproducibility*
- *Linearity/Assay Reportable Range*
- *Detection limit*
- *Analytical Specificity*
- *Assay cut-off*
- *Method Comparison Studies*
- *Clinical Studies (Sensitivity, Specificity, and cut-off)*

9.2 Non-Clinical Performance Testing

9.2.1 *Stability Studies*

Stability studies were conducted on the ADVIA Centaur XP system to support the shelf life unopened and reconstituted material for the ADVIA Centaur FT4 MCMs to ensure that it maintains optimal product performance throughout the established shelf-life. The data supports the stability claims detailed in the ADVIA Centaur FT4 MCM Instructions for Use.

The following stability studies were performed for ADVIA Centaur FT4 MCM:

- Real Time/Shelf Life (Unopened) Stability
- In Use Open Vial (reconstituted) stored at 2–8°C Stability
- On-Board Stability

Real time shelf-life studies (unopened): Test FT4 MCMs were stored unopened at 2–8°C and tested at T=0 and at the following time points: 7 months and 11 months. Real time studies are on-going at T=15 months, 19 months, 24months, 30 months, and 31 months. Shelf life claims are based upon real time stability carried out one month after the duration claimed. Real time shelf-life stability studies of MCMs were determined by comparison of dose recoveries to the -80°C stored reference MCM. The sponsor's acceptance criteria for the real-time stability study were met up to the 7 months' time point, which supports a shelf-life claim of 6 months. Unopened storage shelf-life is indicated by the expiration date on the vial label.

In-Use Open Vial (Reconstituted): Test FT4 MCMs were reconstituted, each level pooled, aliquotted and stored at 2–8°C, tested in 5 replicates per level at T=0, 7, 14, 21, 28, and 29 days. The sponsor's acceptance criteria for the open vial (reconstituted) data supports the open vial claim of 14 days when properly stored at 2–8°C.

On-board Stability: Pooled aliquots of test FT4 MCMs in sample cups were stored on the ADVIA Centaur system and measured at time point T= 0, 2, 4 and 5 hours. The sponsor's acceptance criteria for the on-board stability study were met up to 5 hours, which supports the on-board stability claim for 4 hours.

Stability Acceptance Criteria

The sponsor's stability specifications acceptance criteria for the ADVIA Centaur FT4 MCM are as follows:

- Real Time/Shelf life (Unopened): The dose recovery for MCM1 and the % dose recoveries for MCM2–7 met the sponsor's required acceptance criteria.
- In-Use Open Vial (Reconstituted): The dose recovery for MCM1 and the % dose recoveries for MCM2–7 met the sponsor's required acceptance criteria.
- On-Board: The dose recovery for MCM1 and the % dose recoveries for MCM2–7 met the sponsor's required acceptance criteria.

9.2.2 *Value Assignment*

The ADVIA Centaur FT4 MCMs are value assigned using assigned reference calibrators and MCMs. The assigned reference calibrators are prepared using USP (United States Pharmacopeia) T4 stock and are traceable to USP internal material. The MCMs are manufactured using qualified materials and measurement procedures.

For each new FT4 MCM lot manufactured, MCM1 is run in 5 replicates on two separate runs using one reagent kit lot on the ADVIA Centaur system. A nested testing run protocol is used for MCM2–7 value assignment. This consists of running alternating samples of the reference and new MCM level in the same run. MCM2–7 were tested on 20 replicates in total, comprised of one run and four sample cups run in 5 replicates on one system and one reagent kit lot. This protocol is designed to remove system and run variation. The new MCM doses must fall within the final value assignment specification for FT4 MCMs. The MCMs dose values are generated using the two-point calibration. The new MCM dose is calculated based on the relationship between the observed reference MCM dose and its assigned value. A performance verification run consisting of 6 replicates of each MCM level is run using one instrument, one reagent kit lot and Bio-Rad controls. The mean MCM doses of the new MCM lot manufactured must fall within the customer range specifications.

The target for MCM1 is assigned a 0.0 dose. MCM1 is analyte-free basepool comprising of only the matrix and preservatives. The quality control specifications and final value assignment limits for FT4 MCM ensure that MCM1 measures at or below the FT4 assay sensitivity limit. MCM7 targeted greater than the assay range is diluted with the MCM1 to meet the reportable range of the assay.

9.2.3 *Expected Values*

The expected values are the lot-specific assigned values obtained at value assignment and the lot-specific assigned ranges are the lot-specific customer

ranges are established per the sponsor's internal procedural specifications for FT4 MCM.

ADVIA Centaur FT4 MCM levels and target values are provided in **Table 2.**

Table 2: *Example FT4 MCM Levels and Target Values*

MCM Level	Target Values (ng/dL)
MCM1	0.00
MCM2	0.42
MCM3	0.80
MCM4	1.70
MCM5	3.0
MCM6	5.6
MCM7	13.5
Assay Range	0.1–12.0 ng/dL

9.2.4 *Traceability*

The ADVIA Centaur FT4 assay is standardized to an internal standard manufactured using USP (United States Pharmacopeia) material. Assigned values for calibrators and MCMs are traceable to this standardization.

10. Proposed Labeling

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

11. Conclusion

The ADVIA Centaur FT4 Master Curve Material (MCM) is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the currently marketed IMMULITE 2000 FT4 CVM. Based on the testing completed and the comparisons with predicate device, the ADVIA Centaur FT4 Maser Curve Material does not raise any new questions on safety and effectiveness and the results support a determination of substantial equivalence.

510(k) Summary – ADVIA Centaur T4 Master Curve Material

Introduction: According to the requirements of 21 CFR 807.92, the following information provides sufficient details to understand the basis for determination of substantial equivalence.

The assigned 510(k) Number: k143687

1. Applicant Information	
Mailing Address:	Siemens Healthcare Diagnostics Inc. 511 Benedict Avenue Tarrytown, NY 10591 USA
Contact Person:	Fatima Pacheco Regulatory Clinical Affairs Specialist
Phone Number:	(914) 524-2450
Fax Number:	(914) 524-3579
E-mail Address:	fatima.pacheco@siemens.com
Date Prepared:	July 13, 2015
2. Device Name	
Proprietary Name:	**ADVIA Centaur® T4 Master Curve Material**
Measurand:	Quality Control materials for ADVIA Centaur T4 assay
Type of Test:	Master Curve Material (MCM) for ADVIA Centaur T4 assay
Regulation Section:	21 CFR 862.1660, Quality Control Material
Classification:	Class I Reserved
Products Code:	JJX – Single (Specified) Analyte Controls (Assayed and Unassayed)
Panel:	Clinical Chemistry (75)
3. Predicate Device Name	Elecsys T4 Calcheck 5
Predicate 510(k) No:	k112528
4. Device Description:	ADVIA Centaur® T4 Master Curve Material is an *in vitro* diagnostic product containing various levels of levothyroxine in human plasma with sodium azide and preservatives. Each set contains six levels; with a reconstituted volume of 1.0 mL/vial per level. MCM1 contains no analyte. The T4 MCMs assigned values are lot-specific of target values: 0.00, 2.50, 5.00, 10.0, 15.0, and 35.0 µg/dL.
5. Intended Use:	See Indications for Use Statement below:
Indication for Use:	The ADVIA Centaur® Thyroxine (T4) Master Curve Material is for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur T4 assay.

Special Conditions for Use Statement(s):	For prescription use only
Special Instrument Requirements:	ADVIA Centaur® Systems A description of the ADVIA Centaur system is documented in k971418. Subsequent modifications to the instrument have been reviewed and cleared in k032525 and k041133.
6. Technological Characteristics and Substantial Equivalence Comparison with Predicate:	A comparison of the device features, intended use, and other information demonstrates that the ADVIA Centaur T4 MCM is substantially equivalent to the predicate device as summarized in **Table 1**.

Table 1: *Substantial Equivalence Comparison*

SIMILARITIES		
	Candidate Device	**Predicate Device**
Item	ADVIA Centaur T4 MCM	Elecsys T4 Calcheck 5
Intended Use	The ADVIA Centaur Thyroxine (T4) MCM is for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur T4 assay.	The Elecsys T4 CalCheck 5 is an assayed control for use in calibration verification and for use in the verification of the assay range established by the Elecsys T4 reagent on the indicated Elecsys and **cobas e** immunoassay analyzers.
Analyte	Thyroxine	Same
Form	Lyophilized	Same
Matrix	Human plasma	Human serum
Storage	2–8°C	2–8°C
DIFFERENCES		
Levels	6	5
Stability	**Unopened** – Stable when stored unopened at 2–8°C for 10 months.	**Unopened** – Stored at 2–8°C until the expiration date printed on the bottle labels. **Opened (Reconstituted)** – Stable for 4 hours at 20–25°C.
Use	Single Use Only	Multiple Use

7. Standard/Guidance Document References

The following recognized standard and guidance documents were used:

- Guidance for Industry – Abbreviated 510(k) Submissions for In Vitro Diagnostic Calibrators
- Guidance for Industry and FDA Staff – Assayed and Unassayed Quality Control Material

8. Test Principle

The MCMs are specifically intended for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur assays for use on the ADVIA Centaur systems. Customers may use MCMs for bi-annual calibration verification checks of the assay range and linearity in order to meet the requirements of hospital accreditation bodies.

9. Performance Characteristics

9.1 Analytical performance:

The following studies are not applicable for the purpose of this submission:

- *Precision/Reproducibility*
- *Linearity/Assay Reportable Range*
- *Detection limit*
- *Analytical Specificity*
- *Assay cut-off*
- *Method Comparison Studies*
- *Clinical Studies (Sensitivity, Specificity, and cut-off)*

9.2 Non-Clinical Performance Testing

9.2.1 *Stability Studies*

Stability studies were conducted on the ADVIA Centaur XP system to support the shelf life unopened and reconstituted material for the ADVIA Centaur T4 MCMs to ensure that it maintains optimal product performance throughout the established shelf-life. The data supports the stability claims detailed in the ADVIA Centaur T4 MCM Instructions for Use.

The following stability studies were performed for ADVIA Centaur T4 MCM:

Real time shelf-life studies (unopened): Test T4 MCMs were stored unopened at 2–8°C and tested at T=0 and at the following time points: 7 months and 11 months. Real time studies are on-going at T=15 months, 19 months, 24 months, 30 months, and 31 months. Shelf life claims are based upon real time stability carried out one month after the duration claimed. Real time shelf-life stability studies of MCMs were determined by comparison of dose recoveries to the -80°C stored reference MCM. Acceptance criteria for the real-time stability study were met up to the 11 months' time point, which supports a shelf-life claim of 10 months. Unopened storage shelf-life is indicated by the expiration date on the vial label.

Stability Acceptance Criteria

The sponsor's stability specifications acceptance criteria for the ADVIA Centaur T4 MCM are as follows:

Real Time/Shelf life (Unopened): The dose recovery for MCM1 and the % dose recoveries for MCM2–6 met the sponsor's required acceptance criteria.

9.2.2 *Value Assignment*

The ADVIA Centaur T4 MCMs are value assigned using assigned reference calibrators and MCMs. The assigned reference calibrators are prepared using USP (United States Pharmacopeia) T4 stock and are traceable to USP internal material. The MCMs are manufactured using qualified materials and measurement procedures.

For each new T4 MCM lot manufactured, MCM1 is run in 5 replicates on two separate runs using one reagent kit lot on the ADVIA Centaur system. A nested testing run protocol is used for MCM2–6 value assignment. This consists of running alternating samples of the reference and new MCM level in the same run. MCM2–6 were tested on 20 replicates in total, comprised of one run and four sample cups run in 5 replicates on one system and one reagent kit lot. This protocol is designed to remove system and run variation. The new MCM doses must fall within the final value assignment specification for T4 MCMs. MCM6 is expected to read above the assay range of 30.0 ug/dL, therefore the MCM6 level is also diluted 1:4 before testing. The MCMs dose values are generated using the two-point calibration. The new MCM dose is calculated based on the relationship between the observed reference MCM dose and its assigned value. A performance verification run consisting of 6 replicates of each MCM level is run using one instrument, one reagent kit lot and Bio-Rad controls. The mean MCM doses of the new MCM lot manufactured must fall within the customer range specifications.

The target for MCM1 is assigned a 0.0 ug/dL dose. MCM1 is analyte-free basepool comprising of only the matrix and preservatives. The quality control specifications and final value assignment limits for T4 MCM ensure that MCM1 measures at or below the T4 assay sensitivity limit. MCM6 targeted greater than the assay range is diluted with the MCM1 to meet the reportable range of the assay.

9.2.3 *Expected Values*

The expected values are the lot-specific assigned values obtained at value assignment and the lot-specific assigned ranges are the lot-specific customer ranges are established per the sponsor's internal procedural specifications for T4 MCM.

ADVIA Centaur T4 MCM levels and target values are provided in **Table 2.**

***Table 2: Example** T4 MCM Levels and Target Values*

MCM Level	Target Values (µg/dL)
MCM1	0.00
MCM2	2.50
MCM3	5.00
MCM4	10.0
MCM5	15.0
MCM6	35.0
Assay Range	0.3–30.0 µg/dL

9.2.4 *Traceability*

The ADVIA Centaur T4 assay is standardized to an internal standard manufactured using USP (United States Pharmacopeia) material. Assigned values for calibrators and MCMs are traceable to this standardization.

10. Proposed Labeling

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

11. Conclusion

The ADVIA Centaur T4 Master Curve Material (MCM) is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the currently marketed Elescys T4 Calcheck 5. Based on the testing completed and the comparisons with predicate device, the ADVIA Centaur T4 Maser Curve Material does not raise any new questions on safety and effectiveness and the results support a determination of substantial equivalence.

510(k) Summary – ADVIA Centaur T3 Master Curve Material

Introduction: According to the requirements of 21 CFR 807.92, the following information provides sufficient details to understand the basis for determination of substantial equivalence.

The assigned 510(k) Number: k143687

1. Applicant Information	
Mailing Address:	Siemens Healthcare Diagnostics Inc. 511 Benedict Avenue Tarrytown, NY 10591 USA
Contact Person:	Fatima Pacheco Regulatory Clinical Affairs Specialist
Phone Number:	(914) 524-2450
Fax Number:	(914) 524-3579
E-mail Address:	fatima.pacheco@siemens.com
Date Prepared:	July 13, 2015
2. Device Name	
Proprietary Name:	**ADVIA Centaur® T3 Master Curve Material**
Measurand:	Quality Control materials for ADVIA Centaur T3 assay
Type of Test:	Master Curve Material (MCM) for ADVIA Centaur T3 assay
Regulation Section:	21 CFR 862.1660, Quality Control Material
Classification:	Class I Reserved
Products Code:	JJX – Single (Specified) Analyte Controls (Assayed and Unassayed)
Panel:	Clinical Chemistry (75)
3. Predicate Device Name	Elecsys T3 Calcheck 5
Predicate 510(k) No:	k111552
4. Device Description:	ADVIA Centaur® T3 Master Curve Material is an *in vitro* diagnostic product containing various levels of liothyronine in human plasma with sodium azide and preservatives. Each set contains seven levels; with a reconstituted volume of 1.0 mL/vial per level. MCM1 contains no analyte. The T3 MCMs assigned values are lot-specific of target values: 0.00, 0.42, 0.69, 1.11, 1.65, 3.87, and 7.00 ng/mL.
5. Intended Use:	See Indications for Use Statement below:
Indication for Use:	The ADVIA Centaur® Triiodothyronine (T3) Master Curve Material is for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur T3 assay.

Special Conditions for Use Statement(s):	For prescription use only
Special Instrument Requirements:	ADVIA Centaur® Systems A description of the ADVIA Centaur system is documented in k971418. Subsequent modifications to the instrument have been reviewed and cleared in k032525 and k041133.
6. Technological Characteristics and Substantial Equivalence Comparison with Predicate:	A comparison of the device features, intended use, and other information demonstrates that the ADVIA Centaur T3 MCM is substantially equivalent to the predicate device as summarized in **Table 1**.

Table 1: *Substantial Equivalence Comparison*

SIMILARITIES		
	Candidate Device	**Predicate Device**
Item	ADVIA Centaur T3 MCM	Elecsys T3 Calcheck 5
Intended Use	The ADVIA Centaur Triiodothyronine (T3) MCM is for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur T3 assay.	The Elecsys T3 CalCheck 5 is an assayed control for use in calibration verification and for use in the verification of the assay range established by the Elecsys T3 reagent on the indicated Elecsys and **cobas e** immunoassay analyzers.
Analyte	Triiodothyronine	Same
Form	Lyophilized	Same
Matrix	Human plasma	Human serum
Use	Multiple Use	Same
Storage	2–8°C	2–8°C
DIFFERENCES		
Levels	7	5
Stability	**Unopened** – Stable when stored unopened at 2–8°C for 10 months. **Opened (Reconstituted)** – Stable when stored at 2–8°C for 21days; or on-board for 4 hours.	**Unopened** – Stored at 2–8°C until the expiration date printed on the bottle labels. **Opened (Reconstituted)** – Stable for 4 hours at 20–25°C.

7. Standard/Guidance Document References

The following recognized standard and guidance documents were used:

- Guidance for Industry – Abbreviated 510(k) Submissions for In Vitro Diagnostic Calibrators
- Guidance for Industry and FDA Staff – Assayed and Unassayed Quality Control Material

8. Test Principle

The MCMs are specifically intended for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur assays for use on the ADVIA Centaur systems. Customers may use MCMs for bi-annual calibration verification checks of

the assay range and linearity in order to meet the requirements of hospital accreditation bodies.

9. Performance Characteristics

9.1 Analytical performance:

The following studies are not applicable for the purpose of this submission:

- *Precision/Reproducibility*
- *Linearity/Assay Reportable Range*
- *Detection limit*
- *Analytical Specificity*
- *Assay cut-off*
- *Method Comparison Studies*
- *Clinical Studies (Sensitivity, Specificity, and cut-off)*

9.2 Non-Clinical Performance Testing

9.2.1 *Stability Studies*

Stability studies were conducted on the ADVIA Centaur XP system to support the shelf life unopened and reconstituted material for the ADVIA Centaur T3 MCMs to ensure that it maintains optimal product performance throughout the established shelf-life. The data supports the stability claims detailed in the ADVIA Centaur T3 MCM Instructions for Use.

The following stability studies were performed for ADVIA Centaur T3 MCM:

- Real Time/Shelf Life (Unopened) Stability
- In Use Open Vial (reconstituted) stored at 2–8°C Stability
- On-Board Stability

Real time shelf-life studies (unopened): Test T3 MCMs were stored unopened at 2–8°C and tested at T=0 and at the following time points: 7 months and 11 months. Real time studies are on-going at T=15 months, 19 months, 24months, 30 months, and 31 months. Shelf life claims are based upon real time stability carried out one month after the duration claimed. Real time shelf-life stability studies of MCMs were determined by comparison of dose recoveries to the -80°C stored reference MCM. The sponsor's acceptance criteria for the real-time stability study were met up to the 11 months' time point, which supports a shelf-life claim of 10 months. Unopened storage shelf-life is indicated by the expiration date on the vial label.

In-Use Open Vial (Reconstituted): Test T3 MCMs were reconstituted, each level pooled, aliquotted and stored at 2–8°C, tested in 5 replicates per level at T=0, 7, 14, 21, 28, and 29 days. The sponsor's acceptance criteria for the open vial (reconstituted) stability study were met to the 22 days' time point, which supports the open vial claim of 21 days when properly stored at 2–8°C.

On-board Stability: Pooled aliquots of test T3 MCMs in sample cups were stored on the ADVIA Centaur system and measured at time point T= 0, 2, 4 and 5 hours. The sponsor's acceptance criteria for the on-board stability study were met up to 5 hours, which supports the on-board stability claim for 4 hours.

Stability Acceptance Criteria

The sponsor's stability specifications acceptance criteria for the ADVIA Centaur T3 MCM are as follows:

- Real Time/Shelf life (Unopened): The dose recovery for MCM1 and the % dose recoveries for MCM2–7 met the sponsor's required acceptance criteria.
- In-Use Open Vial (Reconstituted): The dose recovery for MCM1 and the % dose recoveries for MCM2–7 met the sponsor's required acceptance criteria.
- On-Board: The dose recovery for MCM1 and the % dose recoveries for MCM2–7 met the sponsor's required acceptance criteria.

9.2.2 *Value Assignment*

The ADVIA Centaur T3 MCMs are value assigned using assigned reference calibrators and MCMs. The assigned reference calibrators are prepared using USP (United States Pharmacopeia) T3 stock and are traceable to USP internal material. The MCMs are manufactured using qualified materials and measurement procedures.

For each new T3 MCM lot manufactured, MCM1 is run in 5 replicates on two separate runs using one reagent kit lot on the ADVIA Centaur system. A nested testing run protocol is used for MCM2–7 value assignment. This consists of running alternating samples of the reference and new MCM level in the same run. MCM2–7 were tested on 20 replicates in total, comprised of one run and four sample cups run in 5 replicates on one system and one reagent kit lot. This protocol is designed to remove system and run variation. The new MCM doses must fall within the final value assignment specification for T3 MCMs. The MCMs dose values are generated using the two-point calibration. The new MCM dose is calculated based on the relationship between the observed reference MCM dose and its assigned value. A performance verification run consisting of 6 replicates of each MCM level is run using one instrument, one reagent kit lot and Bio-Rad controls. The mean MCM doses of the new MCM lot manufactured must fall within the customer range specifications.

The target for MCM1 is assigned a 0.0 dose. MCM1 is analyte-free basepool comprising of only the matrix and preservatives. The quality control specifications and final value assignment limits for T3 MCM ensure that MCM1 measures at or below the T3 assay sensitivity limit.

9.2.3 *Expected Values*

The expected values are the lot-specific assigned values obtained at value assignment and the lot-specific assigned ranges are the lot-specific customer ranges are established per the sponsor's internal procedural specifications for T3 MCM.

ADVIA Centaur T3 MCM levels and target values are provided in **Table 2.**

Table 2: *Example T3 MCM Levels and Target Values*

MCM Level	Target Values (ng/mL)
MCM1	0.00
MCM2	0.42
MCM3	0.69
MCM4	1.11
MCM5	1.65
MCM6	3.87
MCM7	7.00
Assay Range	0.1–8 ng/mL

9.2.4 *Traceability*

The ADVIA Centaur T3 assay is standardized to an internal standard manufactured using USP (United States Pharmacopeia) material. Assigned values for calibrators and MCMs are traceable to this standardization.

10. Proposed Labeling

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

11. Conclusion

The ADVIA Centaur T3 Master Curve Material (MCM) is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the currently marketed Elescys T3 Calcheck 5. Based on the testing completed and the comparisons with predicate device, the ADVIA Centaur T3 Maser Curve Material does not raise any new questions on safety and effectiveness and the results support a determination of substantial equivalence.